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*THE FOUNDATIONS OF MEDICAL SCIENCE.**

THE extraordinary advance which has characterized nearly every department of science during the past fifty years can hardly be said to have helped the solution of that most important of all problems, the very foundation of natural science—the nature of life. To us engaged in the study of disease and the relief of suffering it is—and from more than one point of view—a fundamental question, one which from the earliest times has been regarded by the medical profession with the keenest interest. Time after time scientific enthusiasts have announced in the most confident terms, and for more than forty years the public have been assured again and again, that at last the mystery had been solved or was so near solution that it might be considered as practically settled. Among scientific workers and thinkers, however, the divergence of opinion as to the real nature of life has been, and is, so great that we are still uncertain how any living thing is formed, how it grows, what is the exact nature of many diseases, and in what manner the action of many of our medicines is to be correctly explained; while, notwithstanding great progress in investigation, many morbid changes and phenomena connected with the healing of wounds and the repair of injuries have yet to be cleared up before we shall be able to say that the nature of vital processes is understood. The very foundations—the first principles of all living nature, the exact differences between the living and the non-living state—have still to be established. Even the broad differences between a particle of matter which is actually living and one that has just

ceased to live have not been ascertained, and our physiology, pathology and medical science rest upon no certain basis. Mental operations have received various explanations, but not one that has been offered adequately accounts for the facts, while vague and uncertain data and conflicting interpretations of facts form the foundations upon which uncertain and perpetually changing philosophy has been constructed. So strong, however, is the conviction of some with regard to the truth of the physical doctrine of life, and the generalization that the living and non-living are one, that not a few would modify our systems of government and education in order to bring them into accordance with certain fanciful speculations upon the religion, morality and civilization of the future when physical doctrines shall be universally accepted and taught.

So determined has been and is the set of opinion against the idea of the operation in living beings of anything in its nature distinct from physical or chemical change that I have long hesitated to press a contrary view, notwithstanding that facts and arguments in all departments of living nature give to it very strong support; while, on the other hand, the favorite doctrines still taught are contrary to all living nature, and to make them popular it has been necessary to invent a new nature—a nature which from the first has been shown to be impossible. Lately, however, a change has come over men's views. Not a few have begun to doubt whether the purely physical doctrine of life is supported by facts, and at last the distinguished President of the Chemical Section at the Ipswich meeting of the British Association has dared, not only to express his doubts concerning the purely physical doctrine of life, but has gone so far as to plead 'for a little more vitality.' I heartily join in his plea, and have for many years hoped that ere long we should be per-

* An introductory lecture delivered at King's College Medical School on October 4th, 1895, by Lionel S. Beale, M. B., F. R. C. P. Lond., F. R. S., Joint Professor of the Principles and Practice of Medicine in King's College, London, and Physician to the Hospital.—Abridged from the report in *The Lancet*.

mitted to admit the operation of a vital, constructing, arranging, guiding and regulating power working in everything that has life. I have endeavored to show exactly where this power operates and upon what, and have drawn attention to the fact that the living matter or 'bioplasm' possesses very similar powers in all living things, from the lowest to the highest. For the most part the plea has been in vain, and overwhelming authority has declared for the opposite view, and that those who differ, being weakest, are to go to the wall.

This question of the nature of life forces itself upon our consideration in all our deeper medical and physiological inquiries and in all attempts to decide upon the foundations of natural knowledge. Not only are intellect, thought and the countless workings of the mind inexplicable upon physical doctrines, but the movements and growth of the very simplest living forms are due to far more than is comprised in purely physical and chemical changes. Is not life-power the real, directing, controlling, regulating and selecting agency in every form of the living? How can we accept the proposition that from non-living atoms and their properties is somehow evolved a power which determines the arrangement of these very atoms, which places them in already determined positions, that tears them away from one another and then brings them within the sphere of their influence so that new and totally different substances result? Could watches and engines make themselves, and multiply, regulate and direct, set themselves in motion, and stop when they willed to do so, some comparison might be made between machines and living matter. I feel sure that all intelligent persons will agree with me in thinking that the time has arrived when this matter should be thoroughly reconsidered. The influence of vitality upon matter as a guiding and directing agency—as a

power by which the elements of matter may be torn away from one another, rearranged and caused to recombine in a way unknown to physics and chemistry—has yet to be recognized, and, if possible, investigated. That this power is transmitted from living particles to lifeless ones, which then live, is certain; equally certain is it that all living matter is clear, transparent, structureless and as colorless as pure water. These are the characters of the simple substance in which vital changes are effected without machinery and without any apparatus. This living matter or bioplasm is, I believe, the foundation of all living nature, the seat of all vital phenomena in health and disease, and the only substance in nature possessing powers correctly termed vital. Is there not evidence that in every kind of living matter the elements of the substance that lives may be separated and rearranged in an order determined beforehand, and in such a manner that definite compounds result and structures evidently designed for definite purposes are formed to do certain work? Have any such phenomena been explained by physics and chemistry? Consider whether any machine has been constructed that can perform work and be kept for any length of time in working order without the designing, regulating, managing power of the living mind. Where is the laboratory that performs chemical operations without the chemist? And where is the matter that can be subjected to analytical and synthetical operations without the intervention of some living agency? And yet it has been affirmed again and again that the living cell is a lifeless laboratory, where work of the most complex kind is carried out without any designing, directing or controlling agency whatever. It is often assumed that substances of chemical simplicity are more easily changed in vital action than bodies of great complexity of composition; but so

far as we have evidence complexity and simplicity of composition are equally overcome by living power. The change seems to be carried out in all cases in the most perfect manner, and very quickly. The view of the building up from simple to complex is not justified. The atoms seem to take up their appointed positions and relations as if impelled by an irresistible power, and according to the same principles in every case, from the lowest to the highest organisms.

The members of the profession and all students are to be congratulated upon the addition, during the past three years, of a new subject to those which have long formed the basis of medical education. The careful study of elementary biology must now be taken up by every medical student in the early part of his course. He has to work with the microscope and to become familiar with the use of instruments for delicate research which were not known to the advanced investigators of fifty years ago. Every student acquires real knowledge of the minute structure of the body, and may form his own conception of the general nature of the wonderful changes characteristic of living things, from the lowest organisms to man himself. I hope you have all seen what happens when a particle of living matter, say, of an amœba, exhibits what we call vital movements, and have observed portions moving away from the general mass. Such portions, becoming detached, begin a new and independent life, taking up nutriment on their own account, and growing like the parent organism from which they have been detached, or have detached themselves, and at length increase and multiply and at last die, like all other things that live. Some have affirmed that this living matter is 'like' a mixture of oil and mucilage, but those who have studied practical elementary biology will not be misled by such a 'likeness.' Would that people generally could also

study some of these simple living organisms and learn the differences between that which lives and assimilates, and grows and dies, and that which does not live. No one who had thought over what he had seen would be persuaded to assent to the proposition that the clear structureless living matter should be regarded as a form of machine, molecular or otherwise. When you examined this living matter under a high power I am sure you must have felt astonished that any one could speak of such a thing as a mechanism or as a laboratory. The moving projections or diverticula just alluded to, like those of leucocytes and pus and mucus corpuscles, are well deserving of your further attentive study. Watch carefully the movements and notice how very clear and transparent is the moving matter. In some you cannot discern a single granule even with the aid of the highest powers, and I think when you do see granules and carefully study their movements you will agree with me in the conclusion that it is not in these visible granules that the moving power resides, but that the visible particles are moved by the clear, soft, structureless substance of which the diverticula consist. The process of growth may continue by the taking up of non-living matter by the transparent, moving, living substance and the communication to it of amœba life, through generations. The process has proceeded for thousands of years, but whether an atom of the matter of the parental organism remains, except for a very short time as a constituent part of the detached descendant, seems to rest upon too fanciful a basis to entitle the living changing matter to be regarded as *immortal*. Think over what you have seen and consider how the wonderful movements are occasioned, how the living matter communicates its powers to the non-living and grows and multiplies. Can it be merely chemical change or me-

chanical action that produces the result? When and what is the machinery said to be present, and how is any 'molecular mechanism' to be demonstrated in such transparent substance? *Authority* alone steps forward and insists upon laws and properties and tendencies, declares to us what we are to believe, and prophecies what our successors will discern in the future.

Before the year 1860, after having carried on observations upon the tissues of plants and animals in many departments of living nature, and from the earliest period of development to the fully formed state and into old age, under the highest magnifying powers (from 700 to more than 2000 diameters) and with great advantages as regards the preparation of specimens, I was led to draw a distinction in each tissue, organ or organism between the living growing formative matter and that which had been formed and could not reproduce itself or give rise to more formed matter. I was gradually led to the general conclusion that every form of the living, growing matter was absolutely distinct from every kind of the resulting formed matter produced by it, and, further, that the influence upon the non-living pabulum was peculiar and belonged to all living matter, but to this only, and that it was not comparable with, or allied to, any other known property, power or action of matter. These conclusions were illustrated in detail and were published in 1861. The preparations were shown to my class of physiology in this College and during lectures at the Royal College of Physicians of London, and further discussed in memoirs published in the Transactions of the Royal Microscopical Society and in several works published at that time and since. It seemed to me that there were no indications whatever of the faintest analogy between the two kingdoms of nature—the living and the non-living—no indications of any gradation from matter in the non-

living state to that of life, while all living matter, from the very lowest to the very highest, exhibited certain common characters, being always colorless, structureless, capable of independent movement as a whole or in part, capable of growth, with a power of selecting certain substances and rejecting others, having structural formative power and powers of affecting chemical change, rendering it certain that the origin of matter so endowed was not direct from the non-living, and that this doctrine sooner or later would have to be abandoned. The warmest advocates of the latter view have never given adequate reasons for the faith they professed, or answered the many objections advanced against the conclusions they accepted and taught. All the particles of living matter actively concerned in the formation of tissues and organs, easily seen under a power of 200 diameters, are less, and most of them considerably less, than the $\frac{1}{1000}$ part of an inch in diameter. In the absence of such living particles nothing can be formed or secreted. If we are to form any accurate conception of the actual phenomena which occur when some of the matter of these minute living particles is resolved into tissue or secretion, it is necessary to study the matter very attentively with the aid of the highest powers, and then we can expect only to learn some of the broader changes which occur. The actual conversion probably occurs in particles of matter far more minute than can be discerned with the highest powers at our disposal. Most important facts, however, have been demonstrated with reference to the movements of many of these bioplasts. Where fibrous or other tissues are formed which are to be laid down in parallel lines the fibre is as it were spun off as the particle of living matter (bioplast) moves upwards or downwards along the tissue already formed, and thus fibre after fibre is added to those already existing. In some

tissues the bioplast moves round and round the cell cavity, thus forming concentric fibres or layers. Such bioplasts, evenly distributed through all the tissues and organs of the body, even in the solid bone, take part in the formation of the tissue around, may exist through life and change very slowly in health, most of them getting smaller as age advances. These are instrumental in establishing the passage of fluid to and fro in the interstices of the tissue. By this continual flow the integrity of the tissue is preserved and the occurrence of degeneration is prevented or postponed. Anything favoring the passage of more nutrient fluid than the very small quantity required by these slowly living particles favors their enlargement they live too fast. They increase in size, and this change is constant in every form of inflammation and fever. With the enlargement there is invariably rise in temperature of the surrounding part and of the blood as it traverses the nearest capillaries. When this change, as in fever, affects the bioplasts of many tissues of the body and is widely distributed, the temperature of the whole volume of blood is, as we know, raised several degrees, but falls with the diminution of the febrile symptoms, as the bioplasts return to their ordinary condition. If in ordinary inflammation the process continues and increases, the bioplasts give off diverticula which may be detached, and at last 'pus corpuscles' result, and the adjacent structures are destroyed. In all pathological changes these bioplasts take part. The health of the body depends upon the normal state of the bioplasts, and movement and changes continue while life lasts. Their life is destroyed by many poisons, notably by hydrocyanic acid, the proportion of 1 in 100,000 in the blood being probably sufficient to destroy the life of adjacent bioplasts in a few seconds. You must have seen multitudes of these bioplasts

disseminated through the tissues which you have examined, and have, no doubt, studied their arrangement in different tissues and organs, though, perhaps, from their being perfectly colorless you may not have regarded them as the most necessary part of the organism. Without them no tissue or organ could have been formed, could have preserved its integrity, or, in case of injury, could have been repaired. They are the life of the body, and without them nothing can live; they constitute the living part of the body—that is, the matter that dies. In cases of fever and inflammation, and in various conditions in which there is increased flow and facilitated access to the bioplasm of nutrient matter in any tissue or organ, one sees, after the altered state has lasted for a short time, arising here and there in various parts of the bioplasm minute dots, which gradually become large enough to be seen easily and are known as nuclei. If the process continues some of them become much larger, and in them new points appear (nucleoli). This is an example of true evolution, as the bodies in question are new centers of living matter, which arise in already existing and perfectly structureless bioplasm.

Not only as long as life lasts is the substance of which living matter is composed in constant movement and portions caused to change in position, but the very elements of the matter, however strongly they may have been united in the non-living condition, are caused to separate, and not only are they rearranged, but they are rearranged in a definite and predetermined manner which differs in different organisms and in different tissues and organs of the same organism. Such movements, of course, can only be represented to the mind, since the movement spoken of and the affected particles themselves are far beyond the present range of our vision, assisted as it may be to the utmost with the

aid of very high magnifying powers. The movements we are considering in very minute particles of living matter take a general direction from center to circumference, and the places of those which have taken a centrifugal course are taken up by the pabulum, the flow of which is centripetal. It is, in fact, in these centers, far removed from our powers of vision, that life power seems to be communicated to the matter, and here the non-living matter begins to live. Life causes elements, however strongly combined, to separate, and overcomes the physical and chemical attractions of elements in combination. Life is able to raise particles above one another in a manner not explained. Of the rearrangement of the component atoms of matter, and of the alteration of their relation to one another during the living state, there can be no doubt, but how this is effected has not yet been ascertained. This rearrangement is different in the different kinds of living matter and results in the production of certain special substances, constant as regards living matter of the same kind under the accustomed natural conditions.

So far, then, we seem to have arrived at this, that the matter of the body actually living can be distinguished from the material which is formed by changes occurring in any portion in which vital phenomena have ceased. For instance, in the growing 'cell' of epithelium the central part is structureless and is alive, and its particles can grow and multiply. The outer part has structure, but no longer manifests vital phenomena. It cannot produce matter like itself, or grow, or select nutriment, or exhibit spontaneous movements. Just at the point where the formed material and the living matter touch, particles of the latter from time to time cease to exhibit vital changes, and the resulting products become formed material which is added to that already produced. Such changes occur everywhere

in living organisms, from the first to the last moment of existence, whether 'high' or 'low,' 'simple' or 'complex.' *Vital change* is one thing, physical and chemical change another, and no particle of matter is the seat of these two classes of changes at the same moment. But there are other wonderful powers associated with the living condition, known to all but understood by no one, some of which I shall now briefly refer to. With regard to the marvellous power which a speck of living matter may transmit without loss to descendants during centuries, only think of this: The oldest variety of pigeon, bred for many generations without loss, and perhaps with improvement, of its remarkable characteristics, and bear in mind not only as regards color, form and number of feathers, but widely diverging from its original progenitors as to the characters of bones, muscles, nerves and other tissues; as to habits, manner and disposition, as to powers of flight—in fact, as to many particulars which would lead us to regard it as a true species far removed from the rock pigeon—in short, having little in common with that species—nevertheless carries, apparently fixed and unalterable in its organization, not a new tendency, but an inalienable compulsion if left to nature for its offspring to revert to the ancestral characteristics; not immediately, but after a few generations its descendants exhibit the original specific characters, having lost all traces of the variety which but a few (often only three or four) generations before might have been regarded as a definite species of pigeon. And, further, think of this, that every rock pigeon, generation after generation, has possessed deeply ingrained, as it were, in its organization the power of transmitting to descendants the capacity of giving origin to any or several varieties of pigeon that are known, and perhaps to many more varieties not dreamt of, and at the same time to every variety

the power of reversion to the original species, if only each individual is allowed to choose its mate as in a natural state. Consider the constancy and, on the other hand, the wonderful plasticity of the organization of this familiar but remarkable bird. Contemplate the wonderful power of change from, and the more wonderful power of reversion to, the original type transmitted through generation after generation and retained through centuries, the only medium being a speck of matter so minute that it would not be indicated by a very delicate balance, and tell me whether you think it probable that the powers referred to are due to the original material properties of the fragment of matter concerned, or whether this acts only as a carrier of the marvelous power belonging to the living world only and originating in the infinite. Never before the present time was there any possibility of approaching the thorough investigation of the important question of life. Our much wider range of knowledge concerning the structure and action of many living organisms widely separated from one another has, in fact, enabled us to consider the question from many new points of view; and, although the issue between contending parties is perhaps more pronounced than ever, the probability of arriving at the truth has immeasurably increased, if, indeed, it has not already reached something approaching certainty. It is curious that, although knowledge of minute structure and of the actual phenomena characteristic of living matter has been widely spread, the important question of the nature of life and its resemblance to and differences from all physical and chemical actions known has only been very imperfectly debated. One would think that the inquiry lay far away from the paths familiar to most educated persons, but the most important points bearing upon the inquiry can now be made intelligible to edu-

cated minds without much difficulty, so that many thoughtful persons may be able to form a judgment of their own, at least concerning the direction in which the truth will probably be discovered.

Among the broad and well-known facts, then, not to be explained by the physical view of vital actions is the vast subject of heredity so remarkable in every department of nature, both for the long periods of time of its continuous operation and for the magnitude and enormous importance of the results when considered in connection with the very minute quantity of matter concerned. Is the transmission of characteristics of minute structural details of extraordinary constancy handed down from generation to generation for hundreds or thousands of years by the very minute particle of matter which we know to be concerned in the process to be attributed to the physical properties and chemical composition of the matter involved or to vital power communicated to this from the immediate predecessor?

We have now followed the phenomena common and peculiar to all living to the seat of their activity in living matter. In centers far more central than our present means of investigation will permit us to penetrate living particles communicate, and without loss, their marvellous powers to some of the recently selected molecules of the non-living pabulum. It would seem that now for a time the ordinary properties of matter are held in suspense or are overcome. Here occur analytical operations of the most stupendous kind, which are carried out very quickly and in the quietest manner, without apparatus or reagents, and without resort to a high temperature. The matter which is the seat of these phenomena is as clear as water, structureless, and composed of very few elements which, if the matter dies, easily take the form of an albuminous substance with fatty matter and salts. During the living state the atoms of the mat-

ter, if there be atoms, may be torn from one another and made to take up new and definite relations, so that by synthesis there arise new substances with new properties, perhaps exhibiting structure and capable of performing purposive action of the most striking and at present inexplicable kind; motion, heat, light, electricity, being manifest in certain cases among other phenomena, while there are present no arrangements, conditions or apparatus such as would enable us to develop these independently of the living. Here, then, as it seems to me, will be found the foundation not only of the principles of physiological, pathological and medical science, but of that of the whole living world as distinguished from the lifeless cosmos. Here we must look for the initiation of all the changes characteristic of the living state. Account must also be taken of these peculiarly vital phenomena in discussions concerning consciousness, thought, and will, and the life that has been, is and is to be. And may we not even hope that by further and deeper study of the phenomena of living matter under the new advantages of demonstration which we enjoy, and which are constantly progressing, some further light may be thrown by the increased skill of investigators of vital phenomena even upon the nature and relationship of material atoms in that boundless world of the non-living which ever has been and must be regarded alike by learned and unlearned with wonder and admiration?

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*THE MAJOR PREMISE IN PHYSICAL
CHEMISTRY.**

CHEMISTRY is essentially an inductive science, mathematics is essentially deduc-

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tive, while physics holds an intermediate position. Yet in our own science, generalizations are reached from time to time, which serve as major premises for syllogistic reasoning. For example, the proposition that each portion of matter has constant weight is at the basis of our knowledge of chemical equivalents as determined by the balance; the isolation of the metals of the alkalis and alkaline earths led to an insight into the nature of salts in general as metallic compounds; and the 'periodic law,' though not expressed in precise mathematical language, is a most fruitful generalization of generalizations.

Physical chemistry, following the logical methods already so largely adopted in physics, is characterized by a readiness to use the major premise. Instead of making a separate experiment to answer each question of fact, the conclusion may often be reached on theoretical grounds, in the same sense as an engineer may demonstrate the stability of the structure he has designed, or the movements of a newly invented machine. What, then, is the leading major premise in modern chemistry? and what shall be the conditions of fruitfulness?

The doctrine of energy, as based upon thermodynamics, embraces the two laws of conservation and correlation; first, energy (while convertible from one form to another) is constant in amount; second, while work may be wholly converted into heat, only a definite fraction of heat can be converted into work. To specify more clearly, if a quantity of heat, H , is received at temperature T (from absolute zero), and if this is converted into work as far as possible by any ideal process until there remains the quantity H' at temperature T' , then the simple theorem holds that the two quantities of heat are proportional to the two temperatures; and of course the difference between heat received, and heat remaining (that is, the work) is proportional to the